REMARKS

Obviousness Rejections

Claims 18-38 were rejected under 35 USC §103(a) as being unpatentable over U.S. Pat. No. 4,552,899 ("Sunshine") (12/10/04 Office Action at 2.)

For the reasons set forth below the rejection, respectfully is traversed.

Sunshine discloses

> Pharmaceutical compositions and methods of using same comprising a non-steroidal anti-inflammatory drug in combination with at least one other active component selected from an antihistamine, decongestant, cough suppressant (antitussive) or expectorant are provided for the relief of cough, cold and cold-like symptoms.

Abstract;

> It is, therefore, a primary object of the present invention to provide pharmaceutical compositions of matter comprising an analgesically effective amount of a non-steroidal anti-inflammatory drug (NSAID) in combination with at least one of an antihistamine, decongestant, cough suppressant, expectorant and, optionally, including pharmaceutically acceptable carriers therefor.

Col. 1;

> The non-steroidal anti-inflammatory drugs (NSAID's) for use in the pharmaceutical compositions and methods of use of the present invention may be selected from any of the following categories:
> (1) The propionic acid derivatives;
> (2) The acetic acid derivatives;
> (3) The fenamic acid derivatives;
> (4) The biphenylcarboxylic acid derivatives; and
> (5) The oxicams.
> Accordingly, the term "NSAID" as used herein is intended to mean any non-narcotic analgesic non-steroidal anti-inflammatory compound, including the pharmaceutically acceptable non-toxic salts thereof, falling within one of the five structural categories above but excluding aspirin, acetaminophen and phenacetin.

Col. 3;

> Of the propionic acid derivatives for use herein, ibuprofen, naproxen, flurbiprofen, fenoprofen, ketoprofen, suprofen, fenbufen, and fluprofen may be mentioned as particularly preferred compounds.
> Of the acetic acid derivatives, presently preferred members include tolmetin sodium, zomepirac, sulindac and indomethacin.
> Of the fenamic acid derivatives, particularly preferred compounds include mefenamic acid and meclofenamate sodium.
> The particularly preferred biphenylcarboxylic acid derivatives for use in the present invention include diflunisal and flufenisal.
> The particularly advantageous oxicams include piroxicam, sudoxicam and isoxicam.

Col. 3;

preferred.

With respect to the dosage amount of the non-steroidal anti-inflammatory drugs in the compositions of the invention, although the specific dose will vary depending upon the age and weight of the patient, the severity of the symptons, the incidence of side effects and the like, for humans, typical effective analgesic amounts of presently preferred NSAID's for use in unit dose compositions of the invention are about 100–500 mg diflunisal, about 25–100 mg zomepirac sodium, about 50–400 mg ibuprofen, most preferably 100–200 mg, about 125–500 mg naproxen, about 25–100 mg flurbiprofen, about 50–100 mg fenoprofen, about 10–20 mg piroxicam, about 125–250 mg mefenamic acid, about 100–400 mg fenbufen or about 25–50 mg ketoprofen; however, greater or lesser amounts may be employed if desired or necessary. With respect to the compounds set forth hereinabove falling within the propionic acid derivative category, suitable dosage ranges for these compounds will generally fall within the range of 25 mg to 600 mg in each unit dose.

A complete description of the various NSAID's, including acceptable analgesically effective amounts thereof for use in unit dose compositions of the present invention also appears in applicants co-pending U.S. application Ser. Nos. 474,358, filed Mar. 11, 1983 and 578,288, filed Feb. 8, 1984, the entire disclosures of which are incorporated herein by reference. Col. 4;

In the pharmaceutical compositions and methods of the present invention, the foregoing active ingredients will be combined with the non-steroidal anti-inflammatory drug(s) and will typically be administered in admixture with suitable pharmaceutical diluents, excipients or carriers (collectively referred to herein as "carrier" materials) suitably selected with respect to the intended form of administration, i.e., oral tablets, capsules, elixirs, syrups, etc. and consistent with conventional pharmaceutical practices. For instance, for oral administration in the form of tablets or capsules, the active drug components may be combined with any oral non-toxic pharmaceutically acceptable inert carrier such as lactose, starch, sucrose, cellulose, magnesium stearate, dicalcium phosphate, calcium sulfate, mannitol, ethyl alcohol (liquid forms) and the like. Moreover, when desired or necessary, suitable binders, lubricants, disintegrating agents and coloring agents can also be incorporated in the mixture. Suitable binders include Col. 5;

starch, gelatin, natural sugars, corn sweeteners, natural and synthetic gums such as acacia, sodium alginate carboxymethylcellulose, polyethylene glycol and waxes. Among the lubricants there may be mentioned for use in these dosage forms, boric acid, sodium benzoate, sodium acetate, sodium chloride, etc. Disintegrators include, without limitation, starch, methylcellulose agar, bentonite, guar gum, etc. Sweetening and flavoring agents and preservatives can also be included where appropriate. Col. 6;

In making the rejection, the Examiner asserted that Sunshine "combines NSAID's such as ibuprofen in doses from 50 to 400 mg or in general propionic acid derivatives of from 25 mg to about 600 mg with pseudoephedrine for use as a preserved syrup formulation (column 12-13, lines 50-9)."(03/09/04 Office Action at 3.) The Examiner further asserted that "[t]he composition is administered in admixture with suitable pharmaceutical diluents, excipients or carriers suitably selected with respect to the intended form of administration, i.e., oral tablets, capsules, elixirs, syrups, etc." (*Id. at 3-4.*)

The Examiner interpreted claims 18-36 as being "drawn to a composition comprising pharmacologically effective amounts of an amine and a non-steroidal anti-inflammatory drug (NSAID), suspended in a liquid medium wherein the suspension comprises at least one suspending agent and taste masking agent and wherein the composition provides an enhanced absorption rate of the amine into the blood of a human compared with a corresponding composition comprising the amine but not the NSAID." (*Id.* at 3.) The Examiner characterized the dependent claims as being "drawn to suspending agents and to dosages of ibuprofen/pseudoephedrine." (*Id.*) Finally, the Examiner asserted that "[c]laims 26-28 and 34-36 are drawn to the enhanced absorption rate indicated by AUC and CMAX." (*Id.*)

1) The Examiner acknowledged, however, that Sunshine differs from the presently claimed invention in that "[i]t does not specifically recite a suspension." (03/09/04 Office Action at 4.)

To fill the acknowledged gap, the Examiner relied upon the fact that ibuprofen is not soluble in water and "as such would necessarily be suspended in [] syrup" (*Id.*)

The Examiner then concluded that "it would have been obvious to one of ordinary skill in the art at the time the invention was made to employ a suspension base." (*Id.*)

More recently, the Examiner specifically admitted that Sunshine does not specifically recite water, but does disclose a liquid formulation in Example 2. (12/10/04 Office Action at 2.) The Examiner places great weight on the term "etc" in Sunshine to reach beyond that which is specifically disclosed, i.e., elixirs and syrups, to net other forms not specifically recited, i.e., suspension. The Examiner admits that Example 2 is an alcoholic elixir formulation, which has, among other things, alcohol. (12/10/04 Office

Action at 2-3.) The Examiner opined that Sunshine "makes it clear that other pharmaceutically acceptable formulations will be apparent to those skilled in the art of pharmaceutical formulations." (*Id.* at 3.) The Examiner concluded that the skilled artisan would know to add a suspending agent to the syrup or elixir formulation when the agent is only sparingly soluble in water." (*Id.*)

As is fundamental, a *prima facie* case of obviousness must be based on facts, "cold hard facts." *In re Freed*, 165 USPQ 570, 571-72 (C.C.P.A. 1970). When the rejection is not supported by facts, it cannot stand. *Ex parte Saceman*, 27 USPQ2d 1472, 1474 (B.P.A.I. 1993).

"Determination of obviousness cannot be based on the hindsight combination of components selectively culled from the prior art to fit the parameters of the patented invention." ATD Corp. v. Lydall, Inc., 159 F.3d 534, 546, 48 USPQ2d 1321, 1329 (Fed. Cir. 1998). There must be a teaching or suggestion within the prior art, within the nature of the problem to be solved, or within the general knowledge of a person of ordinary skill in the field of the invention, to look to particular sources, to select particular elements, and to combine them as combined by the inventor. See Ruiz v. A.B. Chance Co., 234 F.3d 654, 665, 57 USPQ2d 1161, 1167 (Fed. Cir. 2000); ATD Corp, 159 F.3d at 546, 48 USPQ2d at 1329; Heidelberger Druckmaschinen AG v. Hantscho Commercial Prods., Inc., 21 F.3d 1068, 1072, 30 USPQ2d 1377, 1379 (Fed. Cir. 1994) ("When the patented invention is made by combining known components to achieve a new system, the prior art must provide a suggestion or motivation to make such a combination.").

For a *prima facie* case of obviousness to be established, the teachings from the prior art itself must appear to have suggested the claimed subject matter to one of ordinary skill in the art. *See In re Rinehart*, 189 USPQ 143, 147 (CCPA 1976). The mere fact that the prior art could be modified as proposed by the Examiner is not sufficient to establish a *prima facie* case of obviousness. *See In re Fritch*, 23 USPQ 1780, 1783 (Fed. Cir. 1992).

It is respectfully submitted that it is not seen where the record contains any facts to support the Examiner conclusory statement that having ibuprofen, which is water insoluble, in a syrup or an elixir would necessarily lead to the ibuprofen being suspended in the syrup.

While ibuprofen is insoluble in water, it is readily soluble in organic solvents, e.g., alcohol. (See attached Compound No. 4906 Ibuprofen (Merck Index, 13th Ed. 2001). It is not seen where Sunshine specifically discloses any liquid other than alcohol. The fact that ibuprofen is readily soluble in alcohol would prevent an alcohol-ibuprofen combination from being in a suspension because the ibuprofen would be dissolved in the alcohol. Therefore, the fact that Sunshine specifically discloses only an alcohol and elixirs and syrups would not, it is submitted, lead one skilled in the art to make a water-ibuprofen suspension.

For these reasons, the rejection is improper and should be withdrawn.

2) The Examiner acknowledged that Sunshine's disclosed ibuprofen range differs from the range claimed in claims 25 and 33 of the captioned application.

This rejection is improper for the reasons set forth above and should be withdrawn.

3) Regarding claims 26-28 and 34, the Examiner merely concluded that "it is well settled that the recitation of a new intended use for an old product does not make a claim to that old product patentable."

This rejection is improper for the reasons set forth above and should be withdrawn.

Finally, the Examiner is invited to call the applicants' undersigned representative if any further action will expedite the prosecution of the application or if the Examiner has any suggestions or questions concerning the application or the present Response. In fact, if the claims of the application are not believed to be in full condition for allowance, for any reason, the applicants respectfully request the constructive assistance and suggestions of the Examiner in drafting one or more acceptable claims pursuant to MPEP § 707.07(j) or in making constructive suggestions pursuant to MPEP § 706.03 so that the application can be placed in allowable condition as soon as possible and without the need for further proceedings.

Respectfully submitted,

By: /Timothy E. Tracy, Reg. #39,401/
Timothy E. Tracy

Johnson & Johnson
One Johnson & Johnson Plaza
New Brunswick, NJ 08933-7003
(732) 524-6586
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